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                 New FASTA Display Formats Added to USGENE and PCTGEN
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                 INPADOCDB and INPAFAMDB Enriched with New Content
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                 and Features
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                 CAS Registry Number Crossover Limits Increased to
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                 500,000 in Key STN Databases
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NEWS 10
                 PATDPAFULL: Application and priority number formats
                 enhanced
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                 DWPI: New display format ALLSTR available
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                 New Thesaurus Added to Derwent Databases for Smooth
                 Sailing through U.S. Patent Codes
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                 EMBASE Adds Unique Records from MEDLINE, Expanding
                 Coverage back to 1948
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                 Pre-IPC 8 Data Fields
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         APR 07
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=> S L1 AND IL-10

L2 0 L1 AND IL-10

=> S L1 AND CMV

L3 0 L1 AND CMV

=> S (Interleukin-10 OR IL-10) (S) Cytomegalovirus AND pd<=20041126 2 FILES SEARCHED...

L4 114 (INTERLEUKIN-10 OR IL-10) (S) CYTOMEGALOVIRUS AND PD<=20041126

=> Dup Rem L4

PROCESSING COMPLETED FOR L4

L5 53 DUP REM L4 (61 DUPLICATES REMOVED)

ANSWERS '1-21' FROM FILE MEDLINE

ANSWERS '22-26' FROM FILE BIOSIS

ANSWERS '27-52' FROM FILE CAPLUS

ANSWER '53' FROM FILE EMBASE

 \Rightarrow D Kwic L5 1-52

L5 ANSWER 1 OF 53 MEDLINE on STN DUPLICATE 1

TI Human cytomegalovirus-encoded interleukin-10 homolog inhibits maturation of dendritic cells and alters their functionality.

SO Journal of virology, (2004 Aug) Vol. 78, No. 16, pp. 8720-31. Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X. Report No.: NLM-PMC479089.

AB . . . immunity, and prevents the activation and polarization of naive T cells towards protective gamma interferon-producing effectors. We hypothesized that human cytomegalovirus (HCMV) utilizes its viral IL-10 homolog (cmvIL-10) to attenuate DC functionality, thereby subverting the efficient induction of antiviral immune responses. RNA and protein analyses demonstrated. . .

L5 ANSWER 2 OF 53 MEDLINE on STN DUPLICATE 2

 ${\tt TI}$ Shaping phenotype, function, and survival of dendritic cells by cytomegalovirus-encoded ${\tt IL}{\tt -}10$.

SO Journal of immunology (Baltimore, Md.: 1950), (2004 Sep 1) Vol. 173, No. 5, pp. 3383-91.

Journal code: 2985117R. ISSN: 0022-1767. L-ISSN: 0022-1767.

- L5 ANSWER 3 OF 53 MEDLINE on STN DUPLICATE 3
- TI Human cytomegalovirus interleukin-10 downregulates metalloproteinase activity and impairs endothelial cell migration and placental cytotrophoblast invasiveness in vitro.
- SO Journal of virology, (2004 Mar) Vol. 78, No. 6, pp. 2831-40. Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X. Report No.: NLM-PMC353759.
- L5 ANSWER 4 OF 53 MEDLINE on STN DUPLICATE 4
- TI A novel viral transcript with homology to human interleukin-10 is expressed during latent human cytomegalovirus infection.
- SO Journal of virology, (2004 Feb) Vol. 78, No. 3, pp. 1440-7. Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X. Report No.: NLM-PMC321375.
- L5 ANSWER 5 OF 53 MEDLINE on STN DUPLICATE 5
- TI CXCL10 production from cytomegalovirus-stimulated microglia is regulated by both human and viral interleukin-10.
- SO Journal of virology, (2003 Apr) Vol. 77, No. 8, pp. 4502-15. Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X. Report No.: NLM-PMC152158.
- L5 ANSWER 6 OF 53 MEDLINE on STN DUPLICATE 6
- SO AIDS (London, England), (2003 Nov 21) Vol. 17, No. 17, pp. 2445-50.
 - Journal code: 8710219. ISSN: 0269-9370. L-ISSN: 0269-9370.
- AB . . . which coincided with the study visits. METHODS: Blood was obtained at every study visit and was used for measurements of cytomegalovirus cell-mediated immunity (lymphocyte proliferation, IFN-gamma, IL-2, and IL-10 production), cytomegalovirus viral load, CD4 cell count, and HIV viral load. A logistic-normal model was used to analyse outcome data with repeated. . . 0.02] and marginally increased with every log10 RNA copies/ml HIV viral load (OR 2; P = 0.07). CD4 cell counts, cytomegalovirus lymphocyte proliferation, IL-2, and IL-10 did not reach significance as predictors of cytomegalovirus reactivation. However, cytomegalovirus IFN-gamma production significantly decreased the risk of cytomegalovirus reactivation (OR 0.03; P = 0.04). CONCLUSION: Cytomegalovirus-specific IFN-gamma. . .
- L5 ANSWER 7 OF 53 MEDLINE on STN DUPLICATE 7
- TI Cytomegalovirus infection induces production of human interleukin-10 in macrophages.
- SO European journal of clinical microbiology & infectious diseases: official publication of the European Society of Clinical Microbiology, (2003 Dec) Vol. 22, No. 12, pp. 737-41. Electronic Publication: 2003-11-11.
 - Journal code: 8804297. ISSN: 0934-9723. L-ISSN: 0934-9723.
- AB Earlier findings have suggested that the balance between interleukin-10 and tumor necrosis factor alpha levels in serum may influence the outcome of cytomegalovirus infection in renal transplant recipients. Therefore, the aim of the present study was to investigate whether human cytomegalovirus induces interleukin-10 production in macrophages. Experiments using human cytomegalovirus (strain 2006), ultraviolet-inactivated cytomegalovirus, and mock-infected differentiated THP-1 cells with or without ganciclovir or monoclonal anti-tumor necrosis factor alpha antibodies were performed. Cytomegalovirus-infected cells produced significantly higher levels of human interleukin-

- 10 mRNA and interleukin-10 than ultraviolet-inactivated cytomegalovirus or mock-infected cells. The addition of ganciclovir had little effect on interleukin-10 production. Anti-tumor necrosis factor alpha antibodies appeared to reduce the interleukin-10 levels. In conclusion, human cytomegalovirus infection of macrophages induces production of human interleukin-10. This requires viral entry, but not full viral replication.
- L5 ANSWER 8 OF 53 MEDLINE on STN DUPLICATE 8
- TI Crystal structure of human cytomegalovirus IL-10 bound to soluble human IL-10R1.
- Proceedings of the National Academy of Sciences of the United States of America, (2002 Jul 9) Vol. 99, No. 14, pp. 9404-9. Electronic Publication: 2002-07-01.

 Journal code: 7505876. ISSN: 0027-8424. L-ISSN: 0027-8424.

Journal code: 7505876. ISSN: 0027-8424. L-ISSN: 0027-8424. Report No.: NLM-PMC123153.. . .

- AB . . . critical immune and inflammatory responses by way of interactions with its high- (IL-10R1) and low-affinity (IL-10R2) cell surface receptors. Human cytomegalovirus exploits the IL- 10 signaling pathway by expressing a functional viral IL -10 homolog (cmvIL-10), which shares only 27% sequence identity with hIL-10 yet signals through IL-10R1 and IL-10R2. To define the molecular. . .
- L5 ANSWER 9 OF 53 MEDLINE on STN DUPLICATE 9
- SO Blood, (2002 Dec 15) Vol. 100, No. 13, pp. 4521-8. Electronic Publication: 2002-08-01.

 Journal code: 7603509. ISSN: 0006-4971. L-ISSN: 0006-4971.
- AB . . . was found to suppress Aspergillus-specific lymphoproliferation (P = .037) and release of IFN-gamma in culture supernatants (P = .017). In contrast to cytomegalovirus- and tetanus toxoid-specific T-cell responses, Aspergillus-specific T-cell reconstitution late after allogeneic SCT was characterized by low stimulation indices and a low IFN-gamma/IL-10 ratio. In addition, phosphoantigen-reactive V(gamma)9/V(delta)2 T-cell clones from healthy individuals were found to produce significant amounts of tumor necrosis factor. . .
- L5 ANSWER 10 OF 53 MEDLINE on STN DUPLICATE 10
- TI Potent immunosuppressive activities of cytomegalovirus-encoded interleukin-10.
- SO Journal of virology, (2002 Feb) Vol. 76, No. 3, pp. 1285-92. Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X. Report No.: NLM-PMC135865.
- CN 0 (CMV IL-10 protein, Cytomegalovirus); 0 (Immunosuppressive Agents); 0 (Receptors, Interleukin); 0 (Receptors, Interleukin-10); 0 (Recombinant Proteins); 0 (Viral Proteins)
- L5 ANSWER 11 OF 53 MEDLINE on STN DUPLICATE 12
- SO Transplantation, (2001 Aug 27) Vol. 72, No. 4, pp. 699-706. Journal code: 0132144. ISSN: 0041-1337. L-ISSN: 0041-1337.
- AB . . . factors were analyzed by multivariate analysis using the Cox proportional hazards model. RESULTS: Acute graft-versus-host disease was independently associated with IL-10 gene polymorphisms both from the recipient (relative risk=7.9, P<0.0001) and the donor (relative risk=3.5, P=0.02), a donor's positive serology for cytomegalovirus, and HA-1 mismatches in HLA-A*0201 individuals (relative risk=2.8, P=0.05). Chronic graft-versus-host disease was independently associated with IL-6 gene polymorphism from. . .

- SO Journal of virology, (2000 May) Vol. 74, No. 10, pp. 4658-65. Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X. Report No.: NLM-PMC111986.
- AB . . . and NF-IL-6. Elevated Vpr was also shown to increase transcription of the NF-kappaB and NF-IL-6 enhancer-containing viral promoters for HIV, cytomegalovirus, and simian virus 40, as well as increase the expression of IL-6 and IL-10 in primary macrophages and in A549 cells, tumor necrosis factor alpha expression in primary T cells, and IL-6 and gamma. . .
- L5 ANSWER 13 OF 53 MEDLINE on STN DUPLICATE 14
- TI Human cytomegalovirus harbors its own unique IL-10 homolog (cmvIL-10).
- Proceedings of the National Academy of Sciences of the United States of America, (2000 Feb 15) Vol. 97, No. 4, pp. 1695-700.

 Journal code: 7505876. ISSN: 0027-8424. L-ISSN: 0027-8424.

 Report No.: NLM-PMC26498.
- AB We identified a viral IL-10 homolog encoded by an ORF (UL111a) within the human cytomegalovirus (CMV) genome, which we designated cmvIL-10. cmvIL-10 can bind to the human IL-10 receptor and can compete with human IL-10 for binding sites, despite the fact that these two proteins are only 27% identical. cmvIL-10 requires both subunits of the IL-10 receptor complex to induce signal transduction events and biological activities. The structure of the cmvIL-10 gene is unique by itself...
- L5 ANSWER 14 OF 53 MEDLINE on STN DUPLICATE 15
- SO The Journal of rheumatology, (2000 Jul) Vol. 27, No. 7, pp. 1601-5.
 - Journal code: 7501984. ISSN: 0315-162X. L-ISSN: 0315-162X.
- AB . . . complete adjuvant (FCA), followed by immunization of CII in Freund's incomplete adjuvant (FIA) 3 weeks later (CIA mice). The plasmid cytomegalovirus (pCMV) vector encoding IL-10 (pCMV-IL-10) was inoculated intradermally into DBA/1 Lac/J mice (pCMV-IL-10 CIA mice) one week prior to first immunization with CII. CIA mice inoculated with the backbone pCMV vector instead of. . .
- L5 ANSWER 15 OF 53 MEDLINE on STN DUPLICATE 16
- SO American journal of physiology. Lung cellular and molecular physiology, (2000 Nov) Vol. 279, No. 5, pp. L872-7.

 Journal code: 100901229. ISSN: 1040-0605. L-ISSN: 1040-0605.
- AB . . . to induce IL-10 transgene expression in murine lungs for treatment of endotoxin-induced lung inflammation. Gene transfer was performed with a cytomegalovirus (CMV)-IL-10 plasmid with the aid of the liposomal agents LipofectAMINE and N-[1-(2,3-dioleoyl)propyl]-N,N, N-trimethylammonium methylsulfate (DOTAP). Administration of the endotoxin caused a. . .
- L5 ANSWER 16 OF 53 MEDLINE on STN DUPLICATE 17
- TI Primate cytomegaloviruses encode and express an IL- 10-1ike protein.
- SO Virology, (2000 Mar 15) Vol. 268, No. 2, pp. 272-80. Journal code: 0110674. ISSN: 0042-6822. L-ISSN: 0042-6822.
- AB An open reading frame (ORF) with homology to interleukin— 10~(IL-10) has been identified in rhesus cytomegalovirus (RhCMV). The IL-10-like protein is generated from a multispliced, polyadenylated early gene transcript encompassing part of the corresponding UL111A ORF. . .

- TI The role of the tumor necrosis factor system and interleukin-10 during cytomegalovirus infection in renal transplant recipients.
- SO The Journal of infectious diseases, (2000 Jan) Vol. 181, No. 1, pp. 51-7.

 Journal code: 0413675. ISSN: 0022-1899. L-ISSN: 0022-1899.
- AB The effects of cytomegalovirus (CMV) infection on monocyte and T cell activation and the role of the tumor necrosis factor (TNF) system and interleukin (IL)-10 were studied in a prospective

study of 25 renal transplant recipients. Ten patients developed CMV disease (group A), 5 developed. . .

- L5 ANSWER 18 OF 53 MEDLINE on STN DUPLICATE 19
- TI Murine cytomegalovirus infection down-regulates MHC class II expression on macrophages by induction of $\rm IL{-}10$.
- SO Journal of immunology (Baltimore, Md.: 1950), (1999 Jun 1) Vol. 162, No. 11, pp. 6701-7.

 Journal code: 2985117R. ISSN: 0022-1767. L-ISSN: 0022-1767.
- L5 ANSWER 19 OF 53 MEDLINE on STN DUPLICATE 20
- SO Veterinary immunology and immunopathology, (1998 May 15) Vol. 63, No. 1-2, pp. 139-48. Ref: 48
 Journal code: 8002006. ISSN: 0165-2427. L-ISSN: 0165-2427.
- AB . . . responses. Some of the viral defense molecules that interfere with the functions of cytokines include the EBV protein BCRF1 (viral IL-10) which blocks synthesis of cytokines such as IFN-gamma, viral IL-17 and IL-8 receptor encoded by the herpesvirus saimiri genome and chemokine receptor homologues of Epstein-Barr virus, herpesvirus saimiri and cytomegalovirus. These immunomodulatory tactics function to protect the host from the lethal inflammatory effects as well as inhibit the local inflammatory. . .
- L5 ANSWER 20 OF 53 MEDLINE on STN DUPLICATE 21
- SO Journal of immunological methods, (1997 Mar 10) Vol. 202, No. 1, pp. 41-8.

Journal code: 1305440. ISSN: 0022-1759. L-ISSN: 0022-1759.

- AB . . . an immunoadhesin. A recombinant adenovirus, rendered replication defective by deletion of the E1 gene, was constructed to contain the murine interleukin-10 gene fused in frame with the hinge, CH2, and CH3 domains of the murine immunoglobulin gamma 1 heavy chain constant region gene under the control of the human cytomegalovirus promoter. The resultant recombinant virus, Ad5.hCMV.mIL-10:HFc, was used to transduce several cell types. The expressed protein, mIL-10:HFc, is secreted as. . .
- L5 ANSWER 21 OF 53 MEDLINE on STN DUPLICATE 22
- SO The Journal of experimental medicine, (1995 Jun 1) Vol. 181, No. 6, pp. 2289-93.

 Journal code: 2985109R. ISSN: 0022-1007. L-ISSN: 0022-1007.

 Report No.: NLM-PMC2192075.
- AB . . . block its interactions with cellular receptors. Mice were treated intraperitoneally with cationic liposomes containing 200 micrograms of either a pCMV (cytomegalovirus)/p55 expression plasmid that contains the extracellular domain and transmembrane region of the human p55 TNF receptor, or a pcD-SR-alpha/hIL-10 expression plasmid containing the DNA for human interleukin 10. 48 h later, mice were challenged with lipopolysaccharide (LPS) and D-galactosamine. Pretreatment of mice with p55 or IL-10 cDNA-liposome complexes. . .
- L5 ANSWER 22 OF 53 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN

- SO Current Pharmaceutical Design, (2004) Vol. 10, No. 31, pp. 3873 - 3884. print. ISSN: 1381-6128 (ISSN print).
- Major Concepts Biochemistry and Molecular Biophysics

IΤ

- Chemicals & Biochemicals ΙT cytokine; cytomegalovirus interleukin-10 [CMVIL-10]; interferon-lambda-1 [IFN-lambda-1]; interferon-lambda-1-receptor-1 [IFN-lambda-R-1]; interferon-lambda-2 [IFN-lambda-2]; interferon-lambda-3 [IFN-lambda-3]; interleukin-10 [IL-10]: intercalated dimer, six-helix bundle domains, viral gene homologs; interleukin-10.
- ANSWER 23 OF 53 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on L5
- SO Hepatology, (October 2003) Vol. 38, No. 4 Suppl. 1, pp. 462A. print.
- Meeting Info.: 54th Annual Meeting of the American Association for. . . cytometry for activation, memory, differentiation and tissue homing AB. markers. The specificity for hepatitis C virus (HCV), Epstein Barr virus (EBV), cytomegalovirus (CMV), influenza A virus, vaccinia virus peptides and tetanus toxoid protein was analyzed in a 6-h ex vivo stimulation assay followed by intracellular staining for IFN-gamma, TNF-alpha, IL-4 and IL-10. Maturation of CD4/CD8 double-positive cells and CD4 and CD8 single-positive cells was assessed by molecular analysis of T-cell Receptor Excision.
- L5ANSWER 24 OF 53 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on
- CXCL10 production from cytomegalovirus-stimulated human ΤТ microglia: Regulation by interleukin-10.
- SO Journal of Neurovirology, (June, 2002) Vol. 8, No. Supplement 1, pp. 58. print. Meeting Info.: 4th International Symposium of NeuroVirology and the 10th Conference.
- ANSWER 25 OF 53 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on L5
- ΤI Differential effect of cytomegalovirus (CMV) on G-CSF, GM-CSF, IL-6, IL-10 and TGF-beta production by human bone marrow stromal cells.
- SO Experimental Hematology (Charlottesville), (1994) Vol. 22, No. 8, pp. 812. Meeting Info.: 23rd Annual Meeting of the International Society for Experimental Hematology. Minneapolis, Minnesota,.
- ANSWER 26 OF 53 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on L5STN
- Differential effect of cytomegalovirus (CMV) on G-CSF GM-CSF, TΤ IL-6, IL-10 and TGF-beta production by human bone marrow stromal cells.
- British Journal of Haematology, (1994) Vol. 87, No. SUPPL. 1, SO pp. 100. Meeting Info.: First Meeting of the European Haematology Association. Brussels, Belgium. June 2-5,. .
- L5ANSWER 27 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN DUPLICATE 11
- ΤI Reduced expression of HLA class II molecules and interleukin-10- and transforming growth factor β 1-independent suppression of T-cell proliferation in human cytomegalovirus-infected macrophage cultures
- Journal of Virology (2001), 75(11), 5174-5181 SO

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CODEN: JOVIAM; ISSN: 0022-538X
ΙT
     Antigen presentation
     CD4-positive T cell
     Human herpesvirus 5
     Immunosuppression
        (HLA class II mols. expression decrease and interleukin-
        10- and transforming growth factor \beta1-independent
        suppression of T-cell proliferation by human cytomegalovirus
        -infected macrophages)
     Interleukin 10
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (HLA class II mols. expression decrease and interleukin-
        10- and transforming growth factor \beta1-independent
        suppression of T-cell proliferation by human cytomegalovirus
        -infected macrophages)
     Histocompatibility antigens
ΤT
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (HLA-DP; HLA class II mols. expression decrease and interleukin
        -10- and transforming growth factor \beta1-independent
        suppression of T-cell proliferation by human cytomegalovirus
        -infected macrophages)
     Histocompatibility antigens
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (HLA-DQ; HLA class II mols. expression decrease and interleukin
        -10- and transforming growth factor \beta1-independent
        suppression of T-cell proliferation by human cytomegalovirus
        -infected macrophages)
     Histocompatibility antigens
ΤТ
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (HLA-DR; HLA class II mols. expression decrease and interleukin
        -10- and transforming growth factor \beta1-independent
        suppression of T-cell proliferation by human cytomegalovirus
        -infected macrophages)
ΙT
    Macrophage
        (infection; HLA class II mols. expression decrease and
        interleukin-10- and transforming growth factor
        \beta1-independent suppression of T-cell proliferation by human
        cytomegalovirus-infected macrophages)
ΙT
     T cell (lymphocyte)
        (proliferation; HLA class II mols. expression decrease and
        interleukin-10- and transforming growth factor
        \beta1-independent suppression of T-cell proliferation by human
        cytomegalovirus-infected macrophages)
ΙT
     Transforming growth factors
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (\beta 1-; HLA class II mols. expression decrease and
        interleukin-10- and transforming growth factor
        \beta1-independent suppression of T-cell proliferation by human
        cytomegalovirus-infected macrophages)
     ANSWER 28 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L5
SO
     Zhonghua Weishengwuxue He Mianyixue Zazhi (2004), 24(12),
     950-954
     CODEN: ZWMZDP; ISSN: 0254-5101
     . . . overexpression of IL-10. Allitridin up-regulated the expression
AB
     of T-bet mRNA and IFN-\gamma and inhibited the expression of GATA-3 mRNA
     and IL-10 in MCMV infected mice, indicating a TH1
```

dominant state which will enhance the specific cellular immune reactions against cytomegalovirus and be helpful for clearance of cytomegalovirus in host.

IT Interleukin 10

RL: BSU (Biological study, unclassified); BIOL (Biological study) (effects of allitridin on expression of transcription factor T-bet/GATA-3 in mice infected by murine cytomegalovirus)

- L5 ANSWER 29 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
- SO Experimental Gerontology (2004), 39(4), 607-613

CODEN: EXGEAB; ISSN: 0531-5565

IT Antigens

Interleukin 10

RL: BSU (Biological study, unclassified); BIOL (Biological study) (dysfunctional cytomegalovirus-specific CD8+ T cells accumulate in elderly)

- L5 ANSWER 30 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
- SO Medycyna Doswiadczalna i Mikrobiologia (2004), 56(3), 309-316 CODEN: MDMIAZ; ISSN: 0025-8601
- IT Interleukin 10

Interleukin 2

Interleukin 4

Interleukin 5

Tumor necrosis factors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (strain dependence of cytomegalovirus infection-induced formation of Th1/Th2 cytokines)

L5 ANSWER 31 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN

PI WO 2004001424 A1 20031231

	PA:	PATENT NO.					KIND DATE			APPLICATION NO.					DATE				
ΡI	WO 2004001424					A1	_	20031231		WO 2003-GB2739						20030624 <			
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			KG,	KΖ,	MD,	RU,	ΤJ,	TM,	AT,	BE,	ВĠ,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	
			FΙ,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,	
								CM,											
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	AU	2003236922																	
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	US					A1	20060316			US 2005-519044						20050902			

- AB . . . certain infectious agents by administration of epitopes derived from those infectious agents. Epitopes derived from viruses which carry homologues of interleukin 10 (IL-10
 -) in their genome, such as Epstein Barr virus and cytomegalovirus , are particularly suitable for these purposes. Particularly preferred is the use of the EBV LMP1 and LMP2 proteins and epitopes. . .
- L5 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
- SO Journal of Virology (2003), 77(3), 1703-1717

```
ΤТ
     Interleukin 10
    Macrophage inflammatory protein 1\alpha
     Macrophage inflammatory protein 1\beta
     Macrophage inflammatory protein 2
     RANTES (chemokine)
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (cytokine response by infiltrating T-cells in murine
        cytomegalovirus infection of submaxillary salivary gland)
L5
    ANSWER 33 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
     European Journal of Immunology (2003), 33(6), 1528-1538
SO
     CODEN: EJIMAF; ISSN: 0014-2980
ΙT
     Interleukin 10
     Interleukin 12
     Interleukin 6
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (human cytomegalovirus impairs dendritic cell function as a
        novel mechanism of human cytomegalovirus immune escape)
     ANSWER 34 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
     Transplantation Proceedings (2003), 35(4), 1333-1337
SO
     CODEN: TRPPA8; ISSN: 0041-1345
     . . . urine as early markers of the evolution of recipient responses
AΒ
     and transplant function after kidney transplantation was evaluated.
     Increased serum IL-10 levels were associated with severe
     infectious complications and impending graft loss, despite the observation
     that the average IL-10 levels did not correlate with the
    manifestation of any bacterial or cytomegalovirus infection, or
     tumor development, thus a fatal course due to infection was suggested by
     increased IL-10 levels. The high IL-10 levels during
     the early post-transplantation period correlated with the late graft loss
     or septic complications, and.
L5
    ANSWER 35 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
SO
     Scandinavian Journal of Immunology (2003), 57(4), 375-383
     CODEN: SJIMAX; ISSN: 0300-9475
ΙT
     Interleukin 10
     Interleukin 2
     Interleukin 4
     Interleukin 5
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (partial restoration of cytokine profile despite reconstitution of
        cytomegalovirus-specific cell-mediated immunity in HIV-infected
        patients during HAART)
L5
     ANSWER 36 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
SO
     Cellular Immunology (2003), 223(1), 77-86
     CODEN: CLIMB8; ISSN: 0008-8749
     Interleukin 10
ΤТ
     Interleukin 18
     Interleukin 2
     Interleukin 4
     Interleukin 6
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (modulation of cytokine expression by interferon-lpha immunotherapy
        in cytomegalovirus-induced myocarditis)
```

ANSWER 37 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN

L5

CODEN: JOVIAM; ISSN: 0022-538X

```
CODEN: IMLED6; ISSN: 0165-2478
ΤТ
    Interleukin 10
    Interleukin 4
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Cytomegalovirus M43 gene modulates T helper cell response)
    ANSWER 38 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L5
ΤI
    Genetic and functional dissection of rhesus cytomegalovirus
    interleukin-10
SO
     (2002) 140 pp. Avail.: UMI, Order No. DA3065232
    From: Diss. Abstr. Int., B 2003, 63(9), 4039
ST
    Rheus cytomegalovirus interleukin 10
    infection
ΙT
    Infection
        (bacterial; genetic and functional dissection of Rhesus
        cytomegalovirus interleukin-10)
ΙΤ
    Human
    Rhesus cytomegalovirus
        (genetic and functional dissection of Rhesus cytomegalovirus
        interleukin-10)
ΙT
    Interleukin 10
    RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (genetic and functional dissection of Rhesus cytomegalovirus
        interleukin-10)
    ANSWER 39 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L_5
TΙ
    Immunologic activities of Rhesus cytomegalovirus-encoded
    IL-10 and human cytomegalovirus-encoded
    IL-10
PΙ
    WO 2002032457 A1 20020425
    PATENT NO.
                      KIND DATE
                                          APPLICATION NO.
                                                                 DATE
                                           _____
                                         WO 2001-US23942
    WO 2002032457
                         A1 20020425
                                                                 20010730 <--
PΙ
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
            RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
            VN, YU, ZA, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    AU 2001080911
                               20020429
                                         AU 2001-80911
                        Α
                                                                  20010730 <--
                                                                  20010730 <--
                                           US 2001-919224
    US 20020197234
                               20021226
                         A1
    EP 1307228
                                          EP 2001-959344
                               20030507
                                                                  20010730 <--
                         A1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
    US 20050191274
                                          US 2005-57104
                                                                  20050210
                        Α1
                               20050901
ST
    cytomegalovirus interleukin 10 inhibitor
    lymphocyte proliferation
ΙT
    Inflammation
        (Crohn's disease; Rhesus cytomegalovirus-encoded IL
        -10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
    Intestine, disease
ΙT
        (Crohn's; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
    Asthma
ΤТ
    Autoimmune disease
```

Immunology Letters (2003), 88(1), 31-35

SO

```
Blood transfusion
     Graves' disease
     Hepatitis
     Human
     Human herpesvirus 5
     Immune disease
     Inflammation
     Leukemia
     Macaca mulatta
     Multiple sclerosis
     Psoriasis
     Rhesus cytomegalovirus
     Rheumatoid arthritis
     Transplant and Transplantation
        (Rhesus cytomegalovirus-encoded IL-10 and
        human cytomegalovirus-encoded IL-10 in
        treatment of immune disorders)
ΤТ
     Cytokines
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); BIOL (Biological study)
        (Rhesus cytomegalovirus-encoded IL-10 and
        human cytomegalovirus-encoded IL-10 in
        treatment of immune disorders)
ΙT
     Interleukin 1a
     Interleukin 6
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Rhesus cytomegalovirus-encoded IL-10 and
        human cytomegalovirus-encoded IL-10 in
        treatment of immune disorders)
ΙT
     Interleukin 10
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (Rhesus cytomegalovirus-encoded IL-10 and
        human cytomegalovirus-encoded IL-10 in
        treatment of immune disorders)
ΤТ
     Autoimmune disease
     Inflammation
     Thyroid gland, disease
        (autoimmune thyroiditis; Rhesus cytomegalovirus-encoded
        IL-10 and human cytomegalovirus-encoded
        IL-10 in treatment of immune disorders)
ΙT
     Transplant and Transplantation
     Transplant and Transplantation
        (bone marrow; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     Dermatitis
ΤТ
        (contact; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
ΙT
     Eye
        (cornea, transplant; Rhesus cytomegalovirus-encoded
        IL-10 and human cytomegalovirus-encoded
        IL-10 in treatment of immune disorders)
     Transplant and Transplantation
ΙT
        (cornea; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     Allergy
ΤТ
        (delayed hypersensitivity; Rhesus cytomegalovirus-encoded
        IL-10 and human cytomegalovirus-encoded
```

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IL-10 in treatment of immune disorders)
ΤТ
     Toxins
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (endotoxins, shock from; Rhesus cytomegalovirus-encoded
        IL-10 and human cytomegalovirus-encoded
        IL-10 in treatment of immune disorders)
     Liver, disease
ΙT
        (fibrosis; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     Transplant and Transplantation
ΙT
        (graft-vs.-host reaction; Rhesus cytomegalovirus-encoded
        IL-10 and human cytomegalovirus-encoded
        IL-10 in treatment of immune disorders)
ΙT
     Transplant and Transplantation
        (heart; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     T cell (lymphocyte)
TT
        (helper cell/inducer, TH1, -type immunity; Rhesus
        cytomegalovirus-encoded IL-10 and human
        cytomegalovirus-encoded IL-10 in treatment
        of immune disorders)
ΙT
     Fibrosis
        (hepatic; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
ΙT
     Intestine, disease
        (inflammatory; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
TТ
     Autoimmune disease
        (insulin-dependent diabetes mellitus; Rhesus cytomegalovirus
        -encoded IL-10 and human cytomegalovirus
        -encoded IL-10 in treatment of immune disorders)
ΙT
     Diabetes mellitus
        (insulin-dependent; Rhesus cytomegalovirus-encoded IL
        -10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     Transplant and Transplantation
ΤT
        (kidney; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
ΙT
     Transplant and Transplantation
        (liver; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     Transplant and Transplantation
JТ
        (lung; Rhesus cytomegalovirus-encoded IL-10
        and human cytomegalovirus-encoded IL-10
        in treatment of immune disorders)
TТ
     Blood
        (peripheral; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     Mononuclear cell (leukocyte)
ΤТ
        (proliferation of; Rhesus cytomegalovirus-encoded IL
        -10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     Lymphocyte
ΙT
        (proliferation; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
```

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10 in treatment of immune disorders)
     Connective tissue, disease
TT
        (scleroderma; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     Transplant and Transplantation
IT
        (skin; Rhesus cytomegalovirus-encoded IL-10
        and human cytomegalovirus-encoded IL-10
        in treatment of immune disorders)
     Lupus erythematosus
IΤ
        (systemic; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
ΙT
     Shock (circulatory collapse)
        (toxic shock syndrome; Rhesus cytomegalovirus-encoded
        IL-10 and human cytomegalovirus-encoded
        IL-10 in treatment of immune disorders)
ΤТ
     Bone marrow
     Bone marrow
     Heart
     Kidney
     Liver
     Lung
     Skin
        (transplant; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
ΙT
     Inflammation
     Intestine, disease
        (ulcerative colitis; Rhesus cytomegalovirus-encoded
        IL-10 and human cytomegalovirus-encoded
        IL-10 in treatment of immune disorders)
     Eye, disease
TΤ
     Inflammation
        (uveitis; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
ΙT
     Infection
     Respiratory system, disease
        (viral; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
ΙT
     Interferons
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (\gamma; Rhesus cytomegalovirus-encoded IL-
        10 and human cytomegalovirus-encoded IL-
        10 in treatment of immune disorders)
     83869-56-1, Gmcsf
ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Rhesus cytomegalovirus-encoded IL-10 and
        human cytomegalovirus-encoded IL-10 in
        treatment of immune disorders)
     ANSWER 40 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L5
     Potent immunosuppressive activities of cytomegalovirus-encoded
     interleukin-10. [Erratum to document cited in
     CA136:261597]
SO
     Journal of Virology (2002), 76(7), 3585
     CODEN: JOVIAM; ISSN: 0022-538X
     erratum immunosuppression cytomegalovirus interleukin
ST
ΙT
     Histocompatibility antigens
```

```
(HLA-A; immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
        inhibition of MHC antigen expression (Erratum))
     Histocompatibility antigens
TT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (HLA-B; immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
        inhibition of MHC antigen expression (Erratum))
     Histocompatibility antigens
ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (HLA-C; immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
        inhibition of MHC antigen expression (Erratum))
ΙT
     Histocompatibility antigens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (HLA-DR; immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
        inhibition of MHC antigen expression (Erratum))
IT
     Histocompatibility antigens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (HLA-G; immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
        inhibition of MHC antigen expression (Erratum))
ΙT
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (TNF-\alpha; immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
        inhibition of cytokine production (Erratum))
ΙT
     Human
     Human herpesvirus 5
     Immunosuppressants
     Macaca mulatta
     Rhesus cytomegalovirus
        (immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10
        (Erratum))
ΙT
     Interleukin 10
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10
        (Erratum))
TT
     Interleukin 1a
     Interleukin 6
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
        inhibition of cytokine production (Erratum))
TT
     Cell proliferation
     Leukocyte
        (immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
        inhibition of leukocyte proliferation (Erratum))
     Interferons
TΤ
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (\gamma; immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
        inhibition of cytokine production (Erratum))
     83869-56-1, Granulocyte macrophage colony stimulating factor
ΤТ
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (immunosuppressive activities of human and rhesus
        cytomegalovirus-encoded interleukin-10 and
```

RL: BSU (Biological study, unclassified); BIOL (Biological study)

inhibition of cytokine production (Erratum))

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L_5
     ANSWER 41 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
     Gene Therapy (2002), 9(20), 1369-1378
SO
     CODEN: GETHEC; ISSN: 0969-7128
     Interleukin 10
IT
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (coimmunization with type I interferon genes enhances protective
        immunity against cytomegalovirus and myocarditis in gB
        DNA-vaccinated mice)
L5
     ANSWER 42 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
SO
     Immunology and Cell Biology (2002), 80(5), 425-435
     CODEN: ICBIEZ; ISSN: 0818-9641
     Interleukin 10
ΙT
     Interleukin 4
     Interleukin 6
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (type I interferon-A6 and interferon-B naked DNA synergistically
        inhibits cytomegalovirus infection and myocarditis)
     ANSWER 43 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L5
     Effects of TNF\alpha and IL-10 on
ΤI
     cytomegalovirus infection in human embryonic lung fibroblasts
     Zhongguo Bingli Shengli Zazhi (2002), 18(3), 265-268
SO
     CODEN: ZBSZEB; ISSN: 1000-4718
AΒ
     The effects of tumor necrosis factor alpha (TNF\alpha) and
     interleukin-10 (IL-10) on human
     cytomegalovirus AD169 (HCMV AD169) infection in human embryonic
     lung fibroblasts (HEL) were studied, and the ability of the infected HEL
     to. . .
     Interleukin 10
ΤТ
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (effects of TNF\alpha and IL-10 on
        cytomegalovirus infection in human embryonic lung fibroblasts)
ΙT
     Embryo, animal
     Fibroblast
     Human
     Lung
        (human embryonic lung fibroblasts; effects of TNFlpha and IL
        -10 on cytomegalovirus infection in human embryonic
        lung fibroblasts)
IT
     Cytomegalovirus
     Human herpesvirus 5
        (infection with; effects of TNF\alpha and IL-10 on
        cytomegalovirus infection in human embryonic lung fibroblasts)
     ANSWER 44 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L5
ΤI
     Sequence, recombinant production, and diagnostic and therapeutic uses of
     cytomegalovirus IL-10
PI
     WO 2001016153 A1 20010308
     PATENT NO.
                         KIND
                               DATE
                                            APPLICATION NO.
                                                                   DATE
     WO 2001016153
                         A1
                               20010308
                                          WO 2000-US24213
                                                                   20000901 <--
PI
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     The invention provides a DNA mol. (gene cmvIL-10) encoding
AB
     interleukin 10 (IL-10) from
     cytomegalovirus strain AD169. The gene cmvIL-10 (UL111a ORF) is
     located between nucleotides 159678-160364 of the CMV genome (GenBank
     X17403). The invention. . .
     DNA sequence cytomegalovirus gene cmvIL10 interleukin
ST
     10; recombinant prodn cytomegalovirus
     interleukin 10 therapeutic diagnostic use
ΙT
     DNA sequences
        (DNA mol. encoding cytomegalovirus IL-10
        gene (cmvIL-10), sequence and diagnostic and therapeutic uses thereof)
TΤ
     Gene, microbial
     RL: ANT (Analyte); BUU (Biological use, unclassified); PRP (Properties);
     THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study);
     USES (Uses)
        (cmvIL-10; DNA mol. encoding cytomegalovirus IL-
        10 gene (cmvIL-10), sequence and diagnostic and therapeutic
        uses thereof)
ΙT
     Drugs
        (composition; cytomegalovirus IL-10, its
        sequence, recombinant production, and diagnostic and therapeutic uses
        including use in IL-10 mediated therapy)
ΙΤ
     Cytomegalovirus
     Molecular cloning
     Protein sequences
        (cytomegalovirus IL-10, its sequence,
        recombinant production, and diagnostic and therapeutic uses including use
        in IL-10 mediated therapy)
ΤТ
     Plasmid vectors
        (pEF-SPFL-cmv2; cytomegalovirus IL-10,
        its sequence, recombinant production, and diagnostic and therapeutic uses
        including use in IL-10 mediated therapy)
ΙT
     Interleukin 10
     RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU
     (Biological study, unclassified); PRP (Properties); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (viral; cytomegalovirus IL-10, its
        sequence, recombinant production, and diagnostic and therapeutic uses
        including use in IL-10 mediated therapy)
ΙT
     288411-05-2P
                    329086-63-7P
                                   329086-71-7P
     RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU
     (Biological study, unclassified); PRP (Properties); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
        (amino acid sequence; cytomegalovirus IL-10
        , its sequence, recombinant production, and diagnostic and therapeutic uses
        including use in IL-10 mediated therapy)
TT
     329086-62-6
     RL: ANT (Analyte); BUU (Biological use, unclassified); PRP (Properties);
     THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study);
     USES (Uses)
        (nucleotide sequence; DNA mol. encoding cytomegalovirus
        IL-10 gene (cmvIL-10), sequence and diagnostic and
        therapeutic uses thereof)
ΙT
     329088-19-9
                   329088-20-2
                                 329088-21-3
                                               329088-22-4
                                                              329088-23-5
     329088-24-6
                   329088-25-7
                                 329088-26-8
                                                329088-27-9
                                                              329088-28-0
     329088-29-1
                   329088-30-4
                                 329088-31-5
                                               329088-32-6
     RL: PRP (Properties)
        (unclaimed nucleotide sequence; sequence, recombinant production, and
        diagnostic and therapeutic uses of cytomegalovirus IL
        -10)
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```
99549-97-0, Glycoprotein (human herpesvirus 4 19.9-kilodalton protein
ΤТ
                      135114-04-4, Interleukin 10 (human
     moiety reduced)
     clone pH15C precursor reduced)
                                      191290-31-0
                                                    239120-26-4
     RL: PRP (Properties)
        (unclaimed protein sequence; sequence, recombinant production, and
        diagnostic and therapeutic uses of cytomegalovirus IL
        -10)
    ANSWER 45 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L5
     Journal of Immunology (2001), 167(5), 2798-2807
     CODEN: JOIMA3; ISSN: 0022-1767
ΤT
     Cytokines
       Interleukin 10
     Interleukin 13
     Interleukin 4
     Interleukin 5
     RL: BAC (Biological activity or effector, except adverse); BOC (Biological
     occurrence); BSU (Biological study, unclassified); MFM (Metabolic
     formation); BIOL (Biological study); FORM (Formation, nonpreparative);
     OCCU (Occurrence)
        (cytomegalovirus infection and Th1/Th2 cytokine expression
        decreases airway eosinophilia, and enhances mucus production in allergic
        airway disease)
     ANSWER 46 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L_5
     Journal of Investigative Medicine (2001), 49(5), 434-441
SO
     CODEN: JINVFI; ISSN: 1081-5589
ST
     susceptibility cytomegalovirus interleukin 10
     lung infection
     Interleukin 10
TΤ
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); BIOL (Biological study)
        (susceptibility to cytomegalovirus infection may be dependent
        on cytokine response to virus)
L5
    ANSWER 47 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
SO
    Cellular Immunology (2001), 213(1), 52-61
     CODEN: CLIMB8; ISSN: 0008-8749
     Interleukin 10
IT
     Interleukin 6
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (lipopolysaccharide and tumor necrosis factor in modulating murine
        cytomegalovirus-induced myocarditis and expression of)
    ANSWER 48 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L_5
     Cytokine (2000), 12(8), 1163-1170
SO
     CODEN: CYTIE9; ISSN: 1043-4666
     Interleukin 10
TT
     Interleukin 1\beta
     Interleukin 4
     Tumor necrosis factors
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (stimulatory and inhibitory action of cytokines on the regulation of
        human cytomegalovirus IE promoter activity in human vascular
        endothelial cells)
L_5
     ANSWER 49 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
     Journal of Medical Virology (2000), 60(2), 223-229
SO
     CODEN: JMVIDB; ISSN: 0146-6615
     Interleukin 10
ΤТ
```

Interleukin 2

```
Interleukin 4
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
     (Biological study); FORM (Formation, nonpreparative)
        (Th1-type cytokines formation is decreased in kidney transplant
        recipients with active cytomegalovirus infection)
    ANSWER 50 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L5
SO
    Virology (1998), 240(1), 12-26
     CODEN: VIRLAX; ISSN: 0042-6822
     Interleukin 10
ΙT
     RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
     (Biological study); FORM (Formation, nonpreparative)
        (murine cytomegalovirus infection-induced polyclonal B cell
        activation is independent of CD4+ T cells and CD40)
    ANSWER 51 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
L_5
     Experimental Lung Research (1998), 24(1), 3-14
SO
     CODEN: EXLRDA; ISSN: 0190-2148
ΙT
     Interleukin 10
     Interleukin 1B
     Interleukin 6
     Tumor necrosis factors
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (synergistic activation of human cytomegalovirus major
        immediate early promoter by prostaglandin E2 and cytokines)
L_5
    ANSWER 52 OF 53 CAPLUS COPYRIGHT 2010 ACS on STN
     Journal of Infectious Diseases (1996), 174(5), 913-919
SO
     CODEN: JIDIAQ; ISSN: 0022-1899
     Lymphokines and Cytokines
ΙT
     RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
     (Biological study); FORM (Formation, nonpreparative)
        (interleukin 10, imbalance in production of cytokines
        by bone marrow stromal cells following cytomegalovirus
        infection)
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STN INTERNATIONAL SESSION SUSPENDED AT 15:04:07 ON 02 JUN 2010
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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:59:16 ON 02 JUN 2010 11 S SLOBEDMAN/AU OR ABENDROTH/AU OR JENKINS/AU L1

0 S L1 AND IL-10 L2 L3 0 S L1 AND CMV

114 S (INTERLEUKIN-10 OR IL-10) (S) CYTOMEGALOVIRUS AND PD<=2004112 L4

53 DUP REM L4 (61 DUPLICATES REMOVED) L_5

=> D ibib abs L5 1-4, 7, 8, 10, 13, 14, 16, 22, 27

ANSWER 1 OF 53 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004377251 MEDLINE PubMed ID: 15280480 DOCUMENT NUMBER:

Human cytomegalovirus-encoded interleukin TITLE: -10 homolog inhibits maturation of dendritic

cells and alters their functionality.

Chang W L William; Baumgarth Nicole; Yu Dong; Barry Peter A AUTHOR: CORPORATE SOURCE: Center for Comparative Medicine, University of California, Davis, County Road 98 and Hutchison Drive, Davis, CA 95616,

USA.. wlchang@ucdavis.edu

AI49342 (United States NIAID NIH HHS) CONTRACT NUMBER: RR00169 (United States NCRR NIH HHS)

SOURCE: Journal of virology, (2004 Aug) Vol. 78, No. 16,

pp. 8720-31.

Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X.

Report No.: NLM-PMC479089.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200409

ENTRY DATE: Entered STN: 29 Jul 2004

Last Updated on STN: 4 Sep 2004 Entered Medline: 3 Sep 2004

AB Interleukin-10 (IL-10) suppresses the maturation and cytokine production of dendritic cells (DCs), key regulators of adaptive immunity, and prevents the activation and polarization of naive T cells towards protective gamma interferon-producing effectors. We hypothesized that human cytomegalovirus (HCMV) utilizes its viral IL-10 homolog (cmvIL-10) to attenuate DC functionality, thereby subverting the efficient induction of antiviral immune responses. RNA and protein analyses demonstrated that the cmvIL-10 gene was expressed with late gene kinetics. Treatment of immature DCs (iDCs) with supernatant from HCMV-infected cultures inhibited both the lipopolysaccharide-induced ${\tt DC}$ maturation and proinflammatory cytokine production. These inhibitory effects were specifically mediated through the IL-10 receptor and were not observed when DCs were treated with supernatant of cells infected with a cmvIL-10-knockout mutant. Incubation of iDCs with recombinant cmvIL-10

recapitulated the inhibition of maturation. Furthermore, cmvIL-10 had pronounced long-term effects on those DCs that could overcome this inhibition of maturation. It enhanced the migration of mature DCs (mDCs) towards the lymph node homing chemokine but greatly reduced their cytokine production. The inability of mDCs to secrete IL-12 was maintained, even when they were restimulated by the activated T-cell signal CD40 ligand in the absence of cmvIL-10. Importantly, cmvIL-10 potentiates these anti-inflammatory effects, at least partially, by inducing endogenous cellular IL-10 expression in DCs. Collectively, we show that cmvIL-10 causes long-term functional alterations at all stages of DC activation.

L5 ANSWER 2 OF 53 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2004417144 MEDLINE DOCUMENT NUMBER: PubMed ID: 15322202

TITLE: Shaping phenotype, function, and survival of dendritic

cells by cytomegalovirus-encoded IL-

10.

AUTHOR: Raftery Martin J; Wieland Dorte; Gronewald Stefanie; Kraus

Annette A; Giese Thomas; Schonrich Gunther

CORPORATE SOURCE: Institute of Virology, Charite Medical School, Berlin,

Germany.

SOURCE: Journal of immunology (Baltimore, Md.: 1950), (2004

Sep 1) Vol. 173, No. 5, pp. 3383-91.

Journal code: 2985117R. ISSN: 0022-1767. L-ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200409

DOCUMENT NUMBER:

ENTRY DATE: Entered STN: 24 Aug 2004

Last Updated on STN: 22 Sep 2004 Entered Medline: 21 Sep 2004

AΒ Human dendritic cells (DCs) are essential for the antiviral immune response and represent a strategically important target for immune evasion of viruses, including human CMV (HCMV). Recently, HCMV has been discovered to encode a unique IL-10 homologue (cmvIL-10). In this study we investigated the capacity of cmvIL-10 to shape phenotype, function, and survival of DCs. For comparison we included human IL-10 and another IL-10homologue encoded by EBV, which does not directly target DCs. Interestingly, cmvIL-10 strongly activated STAT3 in immature DCs despite its low sequence identity with human IL-10. For most molecules cmvIL-10 blocked LPS-induced surface up-regulation, confirming its role as an inhibitor of maturation. However, a small number of molecules on LPS-treated DCs including IDO, a proposed tolerogenic molecule, showed a different behavior and were up-regulated in response to cmvIL-10. Intriguingly, the expression of C-type lectin DC-specific ICAM-grabbing nonintegrin, a receptor for HCMV infection found exclusively on DCs, was also enhanced by cmvIL-10. This phenotypic change was mirrored by the efficiency of HCMV infection. Moreover, DCs stimulated with LPS and simultaneously treated with cmvIL-10 retained the function of immature DCs. Finally, cmvIL-10 increased apoptosis associated with DC maturation by blocking up-regulation of the antiapoptotic long form cellular FLIP. Taken together, these findings show potential mechanisms by which cmvIL-10 could assist HCMV to infect DCs and to impair DC function and survival.

L5 ANSWER 3 OF 53 MEDLINE on STN DUPLICATE 3 ACCESSION NUMBER: 2004101065 MEDLINE

TITLE: Human cytomegalovirus interleukin-

PubMed ID: 14990702

10 downregulates metalloproteinase activity and impairs endothelial cell migration and placental

cytotrophoblast invasiveness in vitro.

AUTHOR: Yamamoto-Tabata Takako; McDonagh Susan; Chang Hsin-Ti;

Fisher Susan; Pereira Lenore

CORPORATE SOURCE: Department of Stomatology, University of California-San

Francisco, San Francisco, California 94143-0512, USA.

CONTRACT NUMBER: AI46657 (United States NIAID NIH HHS)

AI53782 (United States NIAID NIH HHS) EY13683 (United States NEI NIH HHS) HD30367 (United States NICHD NIH HHS)

SOURCE: Journal of virology, (2004 Mar) Vol. 78, No. 6,

pp. 2831-40.

Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X.

Report No.: NLM-PMC353759.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200404

ENTRY DATE: Entered STN: 2 Mar 2004

Last Updated on STN: 9 Apr 2004 Entered Medline: 8 Apr 2004

AΒ At the uterine-placental interface, fetal cytotrophoblasts invade the decidua, breach maternal blood vessels, and form heterotypic contacts with uterine microvascular endothelial cells. In early gestation, differentiating- invading cytotrophoblasts produce high levels of matrix metalloproteinase 9 (MMP-9), which degrades the extracellular matrix and increases the invasion depth. By midgestation, when invasion is complete, MMP levels are reduced. Cytotrophoblasts also produce human interleukin-10 (hIL-10), a pleiotropic cytokine that modulates immune responses, helping to protect the fetal hemiallograft from rejection. Human cytomegalovirus (CMV) is often detected at the uterine-placental interface. CMV infection impairs cytotrophoblast differentiation and invasion, altering the expression of the cell adhesion and immune molecules. Here we report that infection with a clinical CMV strain, VR1814, but not a laboratory strain, AD169, downregulates MMP activity in uterine microvascular endothelial cells and differentiating-invading cytotrophoblasts. Infected cytotrophoblasts expressed CMV IL-10 (cmvIL-10) mRNA and secreted the viral cytokine, which upregulated hIL-10. Functional analyses showed that cmvIL-10 treatment impaired migration in endothelial cell wounding assays and cytotrophoblast invasion of Matrigel in vitro. Comparable changes occurred in cells that were exposed to recombinant hIL-10 or cmvIL-10. Our results show that cmvIL-10 decreases MMP activity and dysregulates the cell-cell and/or cell-matrix interactions of infected cytotrophoblasts and endothelial cells. MMP activity early in placental development could impair cytotrophoblast remodeling of the uterine vasculature and eventually restrict fetal growth in affected pregnancies.

L5 ANSWER 4 OF 53 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2004023559 MEDLINE DOCUMENT NUMBER: PubMed ID: 14722299

TITLE: A novel viral transcript with homology to human

interleukin-10 is expressed during latent

human cytomegalovirus infection.

AUTHOR: Jenkins Christina; Abendroth Allison; Slobedman Barry CORPORATE SOURCE: Centre for Virus Research, Westmead Millennium Institute

and University of Sydney, Westmead, New South Wales, 2145

Australia.

SOURCE: Journal of virology, (2004 Feb) Vol. 78, No. 3,

pp. 1440-7.

Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X.

Report No.: NLM-PMC321375.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200402

ENTRY DATE: Entered STN: 15 Jan 2004

Last Updated on STN: 25 Feb 2004 Entered Medline: 24 Feb 2004

Human cytomegalovirus (CMV) establishes latent infections in hematopoietic cells such as granulocyte-macrophage progenitors (GM-Ps). During latency the virus is sequestered in a nonreplicating state, although limited transcriptional activity has been previously reported. In this study we sought to further examine viral gene expression during the latent phase of infection. Using an experimental model of latency, primary human GM-Ps were latently infected with CMV strain Toledo and extracted RNA subjected to reverse transcription-PCR by using CMV gene-specific primers. Using this approach, we detected transcription from the UL111.5A region of the viral genome. This transcription was also detected in GM-Ps latently infected with AD169 and Towne strains, indicating that expression was CMV strain independent. Significantly, we detected UL111.5A-region transcripts in mononuclear cells from healthy bone marrow and mobilized peripheral blood allograft donors, demonstrating expression during natural latent infection. Mapping experiments with RNA extracted from latently infected GM-Ps revealed the expression of a novel UL111.5A region transcript with a splicing pattern that differed from that reported during productive infection of permissive cells. This UL111.5A region transcript expressed during latent infection is predicted to encode a 139-amino-acid protein with homology to the potent immunosuppressor interleukin-10 (IL-10) and to the viral IL-10 homolog that is expressed during productive CMV infection. Expression of a latency-associated cmvIL-10 may confer upon the virus an ability to avoid immune recognition and clearance during the latent phase of infection.

L5 ANSWER 7 OF 53 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 2003576750 MEDLINE DOCUMENT NUMBER: PubMed ID: 14610657

TITLE: Cytomegalovirus infection induces production of

human interleukin-10 in macrophages.

AUTHOR: Nordoy I; Rollag H; Lien E; Sindre H; Degre M; Aukrust P;

Froland S S; Muller F

CORPORATE SOURCE: Institute of Microbiology, Rikshospitalet, 0027 Oslo,

Norway.

SOURCE: European journal of clinical microbiology & infectious

diseases : official publication of the European Society of

Clinical Microbiology, (2003 Dec) Vol. 22, No.

12, pp. 737-41. Electronic Publication: 2003-11-11.

Journal code: 8804297. ISSN: 0934-9723. L-ISSN: 0934-9723.

PUB. COUNTRY: Germany: Germany, Federal Republic of

DOCUMENT TYPE: (COMPARATIVE STUDY)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200402

ENTRY DATE: Entered STN: 16 Dec 2003

Last Updated on STN: 21 Feb 2004 Entered Medline: 20 Feb 2004

AB Earlier findings have suggested that the balance between interleukin-10 and tumor necrosis factor alpha levels in serum may influence the outcome of cytomegalovirus infection in

renal transplant recipients. Therefore, the aim of the present study was to investigate whether human cytomegalovirus induces interleukin-10 production in macrophages. Experiments using human cytomegalovirus (strain 2006), ultraviolet-inactivated cytomegalovirus, and mock-infected differentiated THP-1 cells with or without ganciclovir or monoclonal anti-tumor necrosis factor alpha antibodies were performed. Cytomegalovirus-infected cells produced significantly higher levels of human interleukin-10 mRNA and interleukin-10 than ultraviolet-inactivated cytomegalovirus or mock-infected cells. The addition of ganciclovir had little effect on interleukin-10 production. Anti-tumor necrosis factor alpha antibodies appeared to reduce the interleukin-10 levels. In conclusion, human cytomegalovirus infection of macrophages induces production of human interleukin-10. This requires viral entry, but not full viral replication.

L5 ANSWER 8 OF 53 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 2002373101 MEDLINE DOCUMENT NUMBER: PubMed ID: 12093920

TITLE: Crystal structure of human cytomegalovirus

IL-10 bound to soluble human IL-10R1.

AUTHOR: Jones Brandi C; Logsdon Naomi J; Josephson Kristopher; Cook

Jennifer; Barry Peter A; Walter Mark R

CORPORATE SOURCE: Center for Biophysical Sciences and Engineering, Department

of Microbiology, University of Alabama, 1025 18th Street

South, Birmingham, AL 35294, USA.

CONTRACT NUMBER: AI47300 (United States NIAID NIH HHS)

SOURCE: Proceedings of the National Academy of Sciences of the

United States of America, (2002 Jul 9) Vol. 99,

No. 14, pp. 9404-9. Electronic Publication: 2002-07-01.

Journal code: 7505876. ISSN: 0027-8424. L-ISSN: 0027-8424.

Report No.: NLM-PMC123153.

PUB. COUNTRY: United States DOCUMENT TYPE: (IN VITRO)

Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: PDB-1LQS ENTRY MONTH: 200208

ENTRY DATE: Entered STN: 17 Jul 2002

Last Updated on STN: 5 Jan 2003 Entered Medline: 8 Aug 2002

AB Human IL-10 (hIL-10) modulates critical immune and inflammatory responses by way of interactions with its high- (IL-10R1) and low-affinity (IL-10R2) cell surface receptors. Human cytomegalovirus exploits the IL-10 signaling pathway by expressing a functional viral IL-10 homolog (cmvIL-10), which shares only 27% sequence identity with hIL-10 yet signals through IL-10R1 and IL-10R2. To define the molecular basis of this virus-host interaction, we determined the 2.7-A crystal structure of cmvIL-10 bound to the extracellular fragment of IL-10R1 (sIL-10R1). The structure reveals cmvIL-10 forms a disulfide-linked homodimer that binds two sIL-10R1 molecules. Although cmvIL-10 and hIL-10 share similar intertwined topologies and sIL-10R1 binding sites, their respective interdomain angles differ by approximately 40 degrees. This difference results in a striking re-organization of the IL-10R1s in the putative cell surface complex. Solution binding studies show cmvIL-10 and hIL-10 share essentially identical affinities for sIL-10R1 whereas the Epstein-Barr virus IL-10 homolog (ebvIL-10), whose structure is highly similar to hIL-10, exhibits a approximately 20-fold reduction in sIL-10R1 affinity. Our results suggest cmvIL-10 and ebvIL-10

have evolved different molecular mechanisms to engage the $\rm IL{-}10$ receptors that ultimately enhance the respective ability of their virus to escape immune detection.

L5 ANSWER 10 OF 53 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 2002051344 MEDLINE DOCUMENT NUMBER: PubMed ID: 11773404

TITLE: Potent immunosuppressive activities of cytomegalovirus-encoded interleukin-

10.

AUTHOR: Spencer Juliet V; Lockridge Kristen M; Barry Peter A; Lin

Gaofeng; Tsang Monica; Penfold Mark E T; Schall Thomas J

CORPORATE SOURCE: ChemoCentryx, San Carlos, California 94070, USA.

CONTRACT NUMBER: 1-R01-HL57883 (United States NHLBI NIH HHS)

SOURCE: Journal of virology, (2002 Feb) Vol. 76, No. 3,

pp. 1285-92.

Journal code: 0113724. ISSN: 0022-538X. L-ISSN: 0022-538X.

Report No.: NLM-PMC135865.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200202

ENTRY DATE: Entered STN: 25 Jan 2002

Last Updated on STN: 20 Apr 2002 Entered Medline: 12 Feb 2002

AΒ Cytomegalovirus (CMV) has highly evolved mechanisms for avoiding detection by the host immune system. Recently, in the genomes of human and primate CMV, a novel gene comprising segments of noncontiguous open reading frames was identified and found to have limited predicted homology to endogenous cellular interleukin-10 (IL-10). Here we investigate the biological activities of the CMV IL-10-like gene product and show it to possess potent immunosuppressive properties. Both purified bacterium-derived recombinant CMV IL-10 and CMV IL-10 expressed in supernatants of human cells were found to inhibit proliferation of mitogen-stimulated peripheral blood mononuclear cells (PBMCs), with specific activity comparable to that of recombinant human IL-10. In addition, CMV IL-10 expressed from human cells inhibited cytokine synthesis, as treatment of stimulated PBMCs and monocytes with CMV IL-10 led to a marked decrease in production of proinflammatory cytokines. Finally, CMV IL-10 was observed to decrease cell surface expression of both major histocompatibility complex (MHC) class I and class II molecules, while conversely increasing expression of the nonclassical MHC allele HLA-G. These results demonstrate for the first time that CMV has a biologically active IL-10 homolog that may contribute to immune evasion during virus infection.

L5 ANSWER 13 OF 53 MEDLINE on STN DUPLICATE 14

ACCESSION NUMBER: 2000144103 MEDLINE DOCUMENT NUMBER: PubMed ID: 10677520

TITLE: Human cytomegalovirus harbors its own unique

IL-10 homolog (cmvIL-10).

AUTHOR: Kotenko S V; Saccani S; Izotova L S; Mirochnitchenko O V;

Pestka S

CORPORATE SOURCE: Department of Molecular Genetics, University of Medicine

and Dentistry of New Jersey, Robert Wood Johnson Medical School, Piscataway, NJ 08854-5635, USA.. kotenkse@umdnj.edu

CONTRACT NUMBER: 1P30-CA72720 (United States NCI NIH HHS)

R01 AI36450 (United States NIAID NIH HHS) R01-CA46465 (United States NCI NIH HHS)

+

SOURCE: Proceedings of the National Academy of Sciences of the

United States of America, (2000 Feb 15) Vol. 97,

No. 4, pp. 1695-700.

Journal code: 7505876. ISSN: 0027-8424. L-ISSN: 0027-8424.

Report No.: NLM-PMC26498.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200003

ENTRY DATE: Entered STN: 30 Mar 2000

> Last Updated on STN: 30 Mar 2000 Entered Medline: 23 Mar 2000

AB We identified a viral IL-10 homolog encoded by an ORF

(UL111a) within the human cytomegalovirus (CMV) genome, which we

designated cmvIL-10. cmvIL-10 can bind to the human IL-

10 receptor and can compete with human IL-10

for binding sites, despite the fact that these two proteins are only 27%

identical. cmvIL-10 requires both subunits of the IL-10 receptor complex to induce signal transduction events and biological activities. The structure of the cmvIL-10 gene is unique by itself. gene retained two of four introns of the IL-10 gene, but the length of the introns was reduced. We demonstrated that cmvIL-10 is expressed in CMV-infected cells. Thus, expression of cmvIL-10 extends the range of counter measures developed by CMV to circumvent detection and destruction by the host immune system.

ANSWER 14 OF 53 MEDLINE on STN DUPLICATE 15

ACCESSION NUMBER: 2001023850 MEDLINE DOCUMENT NUMBER: PubMed ID: 10914840

Suppression of collagen induced arthritis in mice utilizing TITLE:

plasmid DNA encoding interleukin 10.

Miyata M; Sasajima T; Sato H; Saito A; Saito A; Iriswa A; AUTHOR:

Sato Y; Kasukawa R

CORPORATE SOURCE: Department of Internal Medicine II, Fukushima Medical

University School of Medicine, Japan..

metm@msq.biglobe.ne.jp

SOURCE: The Journal of rheumatology, (2000 Jul) Vol. 27,

No. 7, pp. 1601-5.

Journal code: 7501984. ISSN: 0315-162X. L-ISSN: 0315-162X.

PUB. COUNTRY: Canada

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

Priority Journals FILE SEGMENT:

ENTRY MONTH: 200011

Entered STN: 22 Mar 2001 ENTRY DATE:

Last Updated on STN: 22 Mar 2001 Entered Medline: 16 Nov 2000

AB OBJECTIVE: To investigate the therapeutic efficacy as well as the immunological effects of inoculation of an expression vector encoding interleukin 10 (IL-10) in murine type II collagen induced arthritis (CIA). METHODS: CIA was induced in DBA/1 Lac/J mice by immunization with bovine type II collagen (CII) in Freund's complete adjuvant (FCA), followed by immunization of CII in Freund's incomplete adjuvant (FIA) 3 weeks later (CIA mice). The plasmid cytomegalovirus (pCMV) vector encoding

IL-10 (pCMV-IL-10) was inoculated

intradermally into DBA/1 Lac/J mice (pCMV-IL-10 CIA

mice) one week prior to first immunization with CII. CIA mice inoculated with the backbone pCMV vector instead of pCMV-IL-10(pCMV CIA mice), mice inoculated with the pCMV vector alone, without subsequent immunization

with CII (pCMV-C mice), and mice not subjected to any treatment (C mice) were examined as controls. At the 3rd and 5th week after 2nd immunization with CII, booster injections of CII in FIA were administered. Foot pad thicknesses were measured weekly and the histopathological changes in the ankle joints and the titers of IgG1 (Th2 type) and IgG2a (Th1 type) isotype antibodies to CII were examined at the 10th week. RESULTS: pCMV-IL-10 CIA mice showed lesser foot pad thicknesses (p < 0.01 except at Weeks 1-3), less severe histopathological changes (p < 0.01 or 0.05) and lower IgG2a/IgG1 ratios of antibodies to CII (p <0.01) than CIA mice. CONCLUSION: Inoculation of pCMV-IL-10 suppressed CIA through suppression of the Th 1 type immune response in CIA, and offers promise as a potential therapeutic strategy for rheumatoid arthritis.

L5 ANSWER 16 OF 53 MEDLINE on STN DUPLICATE 17

ACCESSION NUMBER: 2000171829 MEDLINE DOCUMENT NUMBER: PubMed ID: 10704336

TITLE: Primate cytomegaloviruses encode and express an

IL-10-like protein.

AUTHOR: Lockridge K M; Zhou S S; Kravitz R H; Johnson J L; Sawai E

T; Blewett E L; Barry P A

CORPORATE SOURCE: Center for Comparative Medicine, University of

California-Davis, Davis, California, 95616, USA...

kmloefler@ucdavis.edu

CONTRACT NUMBER: P51 RR-AG00169 (United States NCRR NIH HHS)

R01 HD-57883 (United States NICHD NIH HHS)
R01 NS-36859 (United States NINDS NIH HHS)

SOURCE: Virology, (2000 Mar 15) Vol. 268, No. 2, pp.

272-80.

Journal code: 0110674. ISSN: 0042-6822. L-ISSN: 0042-6822.

PUB. COUNTRY: United States

DOCUMENT TYPE: (COMPARATIVE STUDY)

Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals OTHER SOURCE: GENBANK-AF200417

ENTRY MONTH: 200004

ENTRY DATE: Entered STN: 27 Apr 2000

Last Updated on STN: 27 Apr 2000 Entered Medline: 18 Apr 2000

AB An open reading frame (ORF) with homology to interleukin-

10 (IL-10) has been identified in rhesus cytomegalovirus (RhCMV). The IL-10-like protein is generated from a multispliced, polyadenylated early gene transcript encompassing part of the corresponding UL111A ORF of human CMV (HCMV). Immunological analyses confirm expression of the IL-10-like protein both in tissue culture and in RhCMV-infected rhesus macaques. Conserved ORFs were subsequently identified in human, baboon, and African green monkey CMV, and a fully processed transcript has been mapped in fibroblasts infected with the Towne strain of HCMV. The conservation of this previously unrecognized ORF suggests that the protein may play an essential role in primate CMV persistence and pathogenesis.

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ACCESSION NUMBER: 2005:64620 BIOSIS DOCUMENT NUMBER: PREV200500067676

TITLE: Structural features of the interleukin-10 family of

cytokines.

AUTHOR(S): Zdanov, Alexander [Reprint Author]

CORPORATE SOURCE: Macromol Crystallog LabCanc Res Ctr, NCI, Frederick, MD,

21702, USA

zdanov@ncifcrf.gov

SOURCE: Current Pharmaceutical Design, (2004) Vol. 10,

No. 31, pp. 3873-3884. print. ISSN: 1381-6128 (ISSN print).

DOCUMENT TYPE: Article

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TITLE: Reduced expression of HLA class II molecules and

interleukin-10- and transforming

growth factor $\beta1\text{--independent}$ suppression of T-cell proliferation in human cytomegalovirus

-infected macrophage cultures

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After a primary infection, human cytomegalovirus (HCMV) establishes lifelong latency in myeloid lineage cells, and the virus has developed several mechanisms to avoid immune recognition and destruction of infected cells. Here, the authors show that HCMV utilizes 2 different strategies to reduce the constitutive expression of HLA-DR, -DP, and -DQ on infected macrophages and that infected macrophages are unable to stimulate a specific CD4+ T-cell response. Downregulation of the HLA class II mols. was observed in 90% of the donor samples and occurred in 2 phases: at an early [1 day postinfection (dpi)] time point postinfection and at a late (4 dpi) time point postinfection. The early inhibition of HLA class II expression and antigen presentation was not dependent on active virus replication, since UV-inactivated virus induced downregulation of HLA-DR and inhibition of T-cell proliferation at 1 dpi. In contrast, the late effect required virus replication and was dependent on the expression of the HCMV unique short (US) genes US1-9 or US11 in 77% of the samples. HCMV-treated macrophages were completely devoid of T-cell stimulation capacity at 1 and 4 dpi. However, while downregulation of HLA class II expression was rather mild, a 66-90% reduction in proliferative T-cell response was observed This discrepancy was due to undefined soluble factors produced in HCMV-infected cell cultures, which did not include interleukin-10 and transforming growth factor $\beta1$. Thus, HCMV reduces expression of HLA class II mols. on HCMV-infected macrophages and inhibits T-cell proliferation by different distinct pathways.

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